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EXAMINER	
HAWES, PILI ASABI	

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 06/09/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/964,273	BRYNJELSEN ET AL.	
	Examiner	Art Unit	
	Pili A. Hawes	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 March 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19 and 21-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19 and 21-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Summary

Receipt of the Applicant's Request for Continued Examination(s) filed 03-20-2006 is acknowledged. Claims 1-19 and 21-38 are pending in this action. Claims 1-19 and 21-38 are rejected.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-7, 11, 21-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Desai et al. US 5916596.

Desai teaches a method of preparing nanoparticles of pharmacologically active agents by solvent evaporation technique from an oil-in-water emulsion prepared under conditions of high shear forces, such as sonication, high pressure homogenation, etc. Employing albumin as the biologically surface active molecule (col. 5, lines 43-52).

The method comprises the steps of homogenizing a mixture of organic phase and aqueous phase (col. 7, lines 40-50). The organic phase contains a pharmaceutically active ingredient and the aqueous phase contains a biocompatible polymer (col. 7, lines 40-50). The biocompatible polymer is a mixture of the pharmaceutically active agent and albumin (col.8, lines 6-7). This teaching anticipates claims 7 and 11. The mixture is subjected to high shear conditions, such as sonication (col. 7, lines 40-50). This teaching anticipates claims 1-6.

Example 2 discloses a specific embodiment of the invention as claimed by applicant. The pharmaceutically active agent, paclitaxel is dissolved in a water immiscible solvent, methylene chloride (col. 17, lines 20-21). Methylene chloride is a solvent with a vapor pressure higher than water. This teaching anticipates claims 20-22. A solution of albumin is added to the organic phase and the mixture is homogenized

(col. 17, lines 21-24) and a crude emulsion is formed col. 17, line 25). The crude emulsion is sonicated in a 40kHz sonicator cell (col. 17, lines 25-26). This teaching anticipates claims 5 and 23. The solvent is evaporated and the particles are harvested with a particle size of 350-420 nm (col. 17, lines 26-31). The example also discloses that the particles can be reconstituted to the original dispersion by adding water (col. 17, lines 35-36). This teaching anticipated claims 25-29.

The pharmaceutically active ingredients recited in claim 24 are anticipated by teaching of pharmaceutical active ingredients suitable for the process taught by Desai. The specific example of paclitaxel as the active ingredient anticipates claim 24 because paclitaxel is an antineoplastic.

It is well known in the art to use sonication as an organic solvent removal method. It would be obvious to one of ordinary skill in the art that the solvent could be removed without a further evaporation step because Desai teaches that the step is optional (col. 7, lines 52-55). One of ordinary skill in the art would be motivated to use sonication as opposed to other methods of solvent removal because sonication provides a gentler way of removing the solvent, and would reduce the potential for loss of product or damage to the product using other conventional methods of solvent removal, such as high temperature or reduced pressure evaporation.

Claims 1-7, 11, 21-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Desai et al. US 5916596 in view of US 6090406.

Desai has been discussed above. Desai does not specifically teach that sonication is used to evaporate the organic solvent.

Popescu discloses an example of using sonication to remove organic solvent such as ether from the reaction mixture (col. 23, lines 20-21).

It would be obvious to use sonication as a method of evaporation of the solvent from the organic-aqueous solvent phase, one of ordinary skill in the art would look to the prior art for a teaching to support this knowledge, and Popescu provides this teaching.

Claims 1-19 and 21-38 rejected under 35 U.S.C. 103(a) as being unpatentable over Violanto et al. US 4826689 in combination with Parikh US 5922355.

Violanto teaches a method of preparing submicronized particles formed by precipitation of the water insoluble compound into an aqueous solution from organic solution (col. 4, lines 32-37). The particle size is in the range 0.5-1.5 microns (col. 3, line 41). The organic solvent to non-solvent liquid ratio is 1:100 to 100:1 (col. 3, lines 54-56). The reference further teaches using surfactants such as poloxamer, and suggests that any other surfactant known to those of ordinary skill would be suitable (col. 6, lines 50-55). The reference teaches that the mixture is stirred (col. 5, line 21, col. 6, lines 56-60).

Parikh discloses a method of preparing submicronized particles of poorly water soluble pharmaceutically active agents comprising reducing the particle size through sonication, homogenization, milling, micro fluidization and precipitation or recrystallization and precipitation of the compound using antisolvent and solvent precipitation techniques (col. 10, lines 23-29). The steps of the method comprise mixing the water insoluble pharmaceutically active ingredient, a phospholipid, with at least one

nonionic, anionic, or cationic surfactant (col. 10, lines 30-34). Suitable surface-active modifiers used in the invention are listed in column 3, lines 6-30).

Parikh's teaches sonication the composition mixture (col. 4, lines 50-56). A suspension of the particles was made in water (col. 5, 2-3). The particles sizes of the particles were in the range 337-361 nm (col. 5, lines 10-22). Parikh lists types of water insoluble pharmaceutical compounds that would be suitable for this invention (col. 2, lines 52-64). The number weighted particle size range is 63-76 nm (col. 5, lines 20-22).

It would be obvious to one of ordinary skill in the art to use an organic solvent to solubilize a poorly water soluble compound and an anti-solvent such as water to induce precipitation and submicronized particles because Popescu teaches this technique. It would futher be obvious to modify the teaching of Popescu by adding other surfactants known to those or ordinary skill in the art because Popescu suggest to do so, and Parikh provides the teaching that surface active agents such as anionic, nonionic, and cationic surfactants can be used. Sonication as a method of solvent removal is well known in the art.

Claims 1-19 and 21-38 rejected under 35 U.S.C. 103(a) as being unpatentable over Violanto et al. US 4826689 in combination with Parikh US 5922355 in view Popescu US 6090406.

Violanto and Parikh were discussed above.

Popescu is further cited for the teaching that it is well known it the art to use sonication as a method of solvent removal. Popescu discloses an example of using

sonication to remove organic solvent such as ether from the reaction mixture (col. 23, lines 20-21).

Thus it would be obvious to one of ordinary skill in the art to use the sonication method of Parikh in the method of making submicronized particles according to Violanto because Popescu provides this teaching.

Response to Arguments

Applicant's arguments with respect to Desai are not persuasive. Applicants argue that Desai does not teach sonication as a method of removing solvent; however this is a technique that is well known in the art, see reference cited above. The instant claims do not exclude their being a biocompatible cross linked polymer coating the particles, the comprising language of the claims leaves open the possibility that other ingredients, such as a biocompatible polymer could be used in the process. Thus this argument against Desai is not persuasive.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Pili A. Hawes whose telephone number is 571-272-8512. The examiner can normally be reached on 8-4:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on 571-272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

P. A. Hawes
Examiner-1615

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